Rejections under 35 U.S.C. §§ 101 and 112, First Paragraph

The Examiner maintains rejection of claims 25-79 under 35 U.S.C. § 101 as allegedly not being "for reasons of record set forth at pages 3-5 of the previous Office action (Paper No. 10, 9/7/00) and pages 2-6 of the previous Office action (Paper No. 13, 5/8/01)."

Once again, Applicants respectfully disagree and traverse this rejection.

A rejection under 35 U.S.C. § 101 is improper when a person of ordinary skill in the art would find credible disclosed features or characteristics of the invention, or statements made by the applicant in the written description of the invention. *See,* M.P.E.P. §§ 2107.01(II), (III) at 2100-[29-31] (Rev. 1, Feb. 2000). In addition, an applicant need only make *one* credible assertion of utility for the claimed invention to satisfy 35 U.S.C. § 101. *See, e.g., Raytheon v. Roper,* 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983), *cert. denied,* 469 U.S. 835 (1984) ("When a properly claimed invention meets at least one stated objective, utility under 35 U.S.C. § 101 is clearly shown."). *See*, M.P.E.P. at 2100-29. Finding a lack of utility is also improper if a person of ordinary skill in the art would know of a use for the claimed invention at the time the application was filed. M.P.E.P. § 2107.01(II)(B) at 2100-[29-30].

Moreover, the burden is on the Examiner to establish why it is more likely than not that one of ordinary skill in the art would doubt *(i.e.,* "question") the truth of the statement of utility. M.P.E.P. § 2107.01(II)(A) at 2100-[31-32]. Thus, the Examiner must provide evidence sufficient to show that the statement of asserted utility would be considered "false" by a person of ordinary skill in the art. *Id.* The Examiner must also present countervailing facts and reasoning sufficient to establish that a person of ordinary skill would not believe the applicants' assertion of utility. *See id.*; *see also*, *In re Brana,* 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). For the reasons set forth below, the

Examiner has not met the burden that is necessary to establish and maintain a rejection for lack of utility under 35 U.S.C. § 101.

As previously described by Applicants (*see* Paper No. 12, pages 4-5), and contrary to the Examiner's comments, the specification contains statements that clearly and fully describe the function and usefulness of Human Cytokine Polypeptide of the present invention. For example, the specification, at page 3, lines 5-8, teaches that polypeptides of the present invention may stimulate cell proliferation and/or differentiation and may be used to treat, for example, restenosis and/or inflammation. Also, the specification, for example at page 37, lines 7-13, teaches that polypeptides of the invention have further related uses, for example, in the detection of neoplasia, a disorder characterized by abnormal cellular proliferation. Furthermore, the specification, for example at page 56, lines 4-6, teaches that the polypeptide of the invention is expressed in heart, brain, lung, placenta, kidney, skeletal muscle, ovary, testis, prostate, and smooth muscle. Moreover, the specification, for example at page 37, line 15 to page 38, line 13, teaches exemplary methods by which such a disorder may be detected using polypeptides of the invention. Applicants repeat their assertion, that such characterization of the invention is sufficient to constitute a showing of utility as required under 35 U.S.C. § 101.

In support of utilities asserted in the specification as filed, Applicants have previously submitted the teachings of Graf et al. and Oelgeschläger et al. *See* Paper No. 12, pages 5-6. These references teach that Human Cytokine Polypeptide of the present invention shares 100% sequence identity with the human homologue of the *twisted gastrulation* protein from *Drosophila melanogaster*; that in the fruitfly this polypeptide is a secreted protein which functions by direct interaction with Bone Morphogenetic Proteins (BMPs); and that this polypeptide functions by a similar mechanism in vertebrates and in flies. From this evidence, one skilled in the art would appreciate that the pending claims

of the present invention are indeed supported by specific and substantial utilities, which are entirely credible in light of the state of knowledge in the art.

However, the Examiner finds Applicants' assertions of utility to be unconvincing. In dismissing Applicants' arguments, the Examiner states:

> contrary to Applicants' arguments, Applicants assertion of utility is not specific because one of ordinary skill in the art would not conclude that the claimed protein would be expected to have the same biological function in fruit flies, amphibians and humans.

See, Paper No. 18, page 2. Applicants respectfully disagree and point out that one of ordinary skill in the art would conclude that the claimed protein would be expected to have the same biological function in fruit flies, amphibians and humans. In support of this assertion, Applicants submit herewith the teachings of Ross et al. (Nature, 410: pp 479-483. (2001)) as Exhibit A. This reference was published in 2001.

Ross et al. specifically compared the function of *Drosophila melanogaster*, mouse, and human orthologs of the instant polypeptides and demonstrated that each functions in a similar fashion to cause a similar result. *See*, Exhibit A at page 481, Figure 3; and right column, third full paragraph. The authors concluded that such proteins "from different species are functionally equivalent," and they function "to antagonize BMP signalling." *See*, Exhibit A at page 479, right column, lines 4-6. Applicants note that these data, together with the accompanying interpretations by those of skill in the art, are confirmatory of assertions made previously by Applicants and dismissed without basis by the Examiner.

In light of the teachings of Ross et al. and the other evidence of record in the present application, Applicants respectfully point out that polypeptides of the invention regulate cellular proliferation and/or differentiation and may therefore be used, for example, in the detection of neoplasia. Applicants further point out that such a use does

constitute a specific utility, in that not every polypeptide serves to regulate cellular proliferation and/or differentiation; a substantial utility, in that detection of disorders such as neoplasia is of vital importance to patients and physicians; and a credible utility, in that all evidence of record indicates, and none contradicts, that it was possible to successfully detect, diagnose and even treat such conditions at the priority date of the present invention. Accordingly, Applicants respectfully contend that the polypeptides of the present invention are supported by a patentable utility as required under 35 U.S.C. § 101.

The Examiner further states that:

> [t]o grant Applicant a patent on the assertion that the claimed polypeptide may stimulate cell proliferation and/or differentiation, is clearly prohibited by this judicial precedent since the compensation to the public is not commensurate with the monopoly granted.

See, Paper No. 18, page 3. Applicants respectfully disagree with the Examiner's reasoning.

Preliminarily, it is unclear to Applicants which judicial precedent is being referenced by the Examiner. Applicants respectfully point out that there are many judicial precedents. Furthermore, Applicants respectfully point out that proportionality of public compensation to monopoly granted is not listed in the M.P.E.P. as a consideration to be weighed in examining an application under 35 U.S.C. § 101. Accordingly, Applicants contend that in the instant case the Examiner's reasoning is unsound and that therefore the present rejection should be reconsidered and withdrawn.

The Examiner contends that "the instant protein has no demonstrated function," and therefore seems to base the present rejection of the invention on a requirement for disclosure of the details of how or why the invention works. *See*, Paper No. 18, page 3. Preliminarily, Applicants point out that the instant protein does indeed have a well-known function as demonstrated by the teachings of Ross et al. and other evidence of record in

the present application. Furthermore, Applicants respectfully but emphatically note that this assertion is contrary to well established law. The Federal Circuit has recently stated with respect to the rejection of claims for lack of utility that:

> "It is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works." Newman v. Quigg, 877 F.2d 1575, 1581, 11 U.S.P.Q.2D (BNA) 1340, 1345 (Fed. Cir. 1989); see also Fromson v. Advance Offset Plate, Inc., 720 F.2d 1565, 1570, 219 U.S.P.Q. (BNA) 1137, 1140 (Fed. Cir. 1983) ("It is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests."). Furthermore, statements that a physiological phenomenon was observed are not inherently suspect simply because the underlying basis for the observation cannot be predicted or explained.

In re Cortright, 49 U.S.P.Q.2d 1464, 1466 (Fed. Cir. 1999). Likewise, according to the axiom of patent law, the utilities asserted for the Human Cytokine Polypeptide do not depend on a precise disclosure of its biological activity. Rather, the issue is whether an asserted utility is true.

The Examiner further claims, that "the instant situation is directly analogous to that which was addressed in *Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966)*... ." See, Paper No. 18, page 5.

Applicants respectfully disagree and point out that at issue in *Brenner v. Manson* was whether a process was patentable, where the product of said process had no demonstrable utility. In *Brenner v. Manson* the "respondent himself recognized that the presumption that adjacent homologues have the same utility has been challenged in the steroid field because of 'a greater known unpredictability of compounds in that field.'" In stark contrast, the present case involves a Human Cytokine polypeptide which has been identified as a human homolog of *twisted gastrulation*, a protein which binds BMPs thereby regulating cellular proliferation and differentiation. The function of Human

Cytokine Polypeptide has been clearly described by, for example, Ross et al. who demonstrate that Applicants previous assertions were in fact true. Therefore, in contrast to the situation in *Brenner v. Manson*, the present invention describes a Human Cytokine Polypeptide whose function has been characterized using routine techniques and whose asserted utility is entirely credible to one of skill in the art.

Other than reiteration of conclusory statements that the invention lacks utility, the Examiner has presented no arguments as to why this asserted utility is not credible. In arguing that Applicants' asserted utility is not credible, the Examiner has not attacked (a) the logic underlying the assertion as seriously flawed or (b) the facts upon which the assertion is based as inconsistent with the logic underlying the assertion. *See*, Revised Interim Utility Guidelines Training Materials, p. 5. In the instant rejection, the Examiner has set forth no arguments as to why Applicants' logic (that Human Cytokine Polypeptide of the present invention has the activity of modulating cell proliferation and/or differentiation) is flawed or that the facts upon which the logic is based on, are inconsistent with the underlying assertion. Thus, the Examiner has failed to make even a *prima facie* showing that Applicants' asserted utility is not credible. Once more, Applicants respectfully submit that the Human Cytokine Polypeptide of the invention (such as, for example, the polypeptide shown as SEQ ID NO:2), has an immediate and specific utility. Such polypeptide may regulate cell proliferation and/or differentiation and therefore, polypeptides of the instant invention, or agonists or antagonists thereof, may be used to treat and/or prevent and/or detect disorders of cell differentiation and/or proliferation such as, for example, neoplasia. Thus, polypeptides of the invention are supported by an immediate utility that is both specific and substantial.

In summary, these asserted utilities for Human Cytokine Polypeptide are specific (not every protein modulates cell proliferation and/or differentiation) and substantial ("the

general rule [is] that the treatments of specific diseases or conditions meet the criteria of 35 U.S.C. § 101." (Revised Interim Utility Guidelines Training Materials, p. 6)). In addition, these utilities are credible and evidentiary support for this credibility has been provided (*See* Paper No. 12). The Examiner has failed, however, to provide any countervailing statements as to why these particular utilities are not specific, substantial and credible.

In regard to asserted therapeutic activities, the Examiner further states "[e]ven if one identifies an agonist or antagonist for a protein of the instant invention, this information is useless since one has no idea of what clinical effect the administration of that agonist or antagonist to an individual would have." The Examiner proceeds to cite extensively from M.P.E.P. § 2138.05 ("CLAIMED INVENTION IS NOT ACTUALLY REDUCED TO PRACTICE UNLESS THERE IS A KNOWN UTILITY" and "A PROBABLE UTILITY MAY NOT BE SUFFICIENT TO ESTABLISH UTILITY") See, Paper No. 18, pages 6-7. Applicants respectfully but strongly disagree.

Preliminarily, Applicants respectfully point out that M.P.E.P. § 2138.05 is a subsection of M.P.E.P. § 2138, which section is concerned with interpretation of 35 U.S.C § 102(g) and interference practice. The Examiner appears to have based the instant rejection, at least in part, on paragraphs of M.P.E.P. § 2138.05 which deal specifically with the requirements for establishment of an actual reduction to practice of an invention in the context of an interference proceeding. However, as indicated in the M.P.E.P.:

> Reduction to practice may be an actual reduction or a constructive reduction to practice which occurs when a patent application on the claimed invention is filed. The filing of a patent application serves as conception and constructive reduction to practice of the subject matter described in the application. Thus the inventor need not provide evidence of either conception or actual reduction to practice when relying on the content of the patent

application. *Hyatt v. Boone*, 146 F.3d 1348, 1352, 47 USPQ2d 1128, 1130 (Fed. Cir. 1998).

See, M.P.E.P. § 2138.05 [2100-107]. Applicants respectfully note that an actual reduction to practice is not required in the present case where: (a) the instant claims are not the subject of an interference proceeding; and (b) the content of the patent application, i.e. a constructive reduction to practice, is being relied upon. Accordingly, Applicants respectfully contend that the Examiner has misapplied the directions given in M.P.E.P. §2138.05 and that the requirements of 35 U.S.C. § 101 have been fully met in the instant case.

Further, Applicants note that there is no need to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty or provide actual evidence of success in treating humans where such a utility is asserted. M.P.E.P. § 2107.02 (I) at 2100-[33-34]. All that is required of Applicants is that there be a reasonable correlation between the biological activity and the asserted utility. *See*, *Nelson v. Bowler*, 626 F.2d 853, 857 (C.C.P.A. 1980). Moreover, "[u]sefulness in patent law, and in particular in the context of pharmaceutical inventions, *necessarily* includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans." *In re Brana, 51* F.3d *1560, 1568* (Fed. Cir. 1995) (emphasis added).

Even assuming, *arguendo,* the Examiner has established a *prima facie* showing that the claimed invention lacks utility, Applicants respectfully submit that they have rebutted the Examiner's showing by proffering sufficient evidence to lead one skilled in the art to conclude that the asserted utilities are more likely than not true. Applicants have directed the Examiner to the specification where clear and specific assertions are made of Human Cytokine polypeptide biological and therapeutic activity.

In view of the above, Applicants submit that the asserted utilities of the invention meet the statutory requirement set forth in 35 U.S.C. § 101. The Examiner has failed to establish and maintain grounds as to why a rejection for lack of utility is proper. Accordingly, Applicants respectfully request that the rejection of claims 25-79 under 35 U.S.C. § 101 be withdrawn.

The Examiner has also rejected claims 25-79 under 35 U.S.C. § 112, first paragraph, "since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention".

Applicants respectfully disagree and traverse this rejection.

As detailed above, the asserted utilities of the invention meet the statutory requirement set forth in 35 U.S.C. § 101 and, armed with the specification of the instant invention, one skilled in the art clearly would know how to use the claimed invention. Accordingly, Applicants respectfully request that the rejection of claims 25-79 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Conclusion

Applicants respectfully request consideration and entry of the foregoing remarks into the file. Applicants believe that no fee is due in connection herewith; however, should the Patent Office determine otherwise, please charge the required fee to Human Genome Sciences, Inc., Deposit Account No. 08-3425.

Respectfully submitted,

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Enclosures
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